IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Marie Bendix HANSEN *et al.*
Title:	**METHOD FOR HIGH THROUGHPUT VOLUMES IN THE FRACTIONATION OF BIO-MOLECULES BY CHROMATOGRAPHIC SYSTEMS**
Appl. No.:	10/548,403
371(c) Date:	7/27/06
Examiner:	Alexander D. Kim
Art Unit:	1656
Confirmation Number:	7935

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Thierry Burnouf, declare the following:

1. I received a Bachelor of science in 1976, a Master of Science in 1977, and a PhD in Plant and Microbial Production in 1981, all from the Université des Sciences et Techniques de Lille, Lille, France. I performed post-doctoral research studies at the Northern Regional Research Center, US Department of Agriculture, Peoria, Illinois, USA from September 1981 to September 1984. I have worked as a research scientist in the field of chromatography for the past 28 years, first as Post-doctoral Research Assistant at the Northern Regional Research Center, US Department of Agriculture, Peoria, Illinois, USA, and subsequently with the plasma fractionation plant of the Centre Régional de Transfusion Sanguine de Lille (Regional Blood Transfusion Center, Lille) as Head of the Research and Development Laboratory, and as Director of the Plasma Fractionation Department and Laboratoire Français du Fractionnement et des Biotechnologies as Scientific Director. I have also been involved in research

and development work using chromatography with Haemonetics Corporation, Braintree, USA, as Vice-President and Director of Haemonetics Plasma Product Services (HPPS). I am presently and since 1998 the Director of Human Protein Process Sciences (formerly names Human Plasma Product Services) based in Lille, France, a consulting company providing services for technology developments. I have spent much of my career developing chromatographic processes for purifying biomolecules and I have over 100 publications and over 20 international patents in the field of biological products and plant and human protein purification. I am a Consultant to the World Health Organization on issues related to human plasma products and I am on the Editorial Board of Biologicals, the journal of the International Association of Biologicals.

2. I have no ownership interest in the captioned application, U.S. serial No. 10/548,403, and I have no personal interest in how the U.S. PTO disposes of the application.

3. I have reviewed the application and related PTO actions, respectively dated October 29, 2008, and March 31, 2009. I understand that the examiner found claims 1-15 of the application unpatentable in part because, in his estimation, the specification does not describe the claimed subject matter of the application in such a way as to reasonably convey to a person skilled in bio-molecule fractionation that, when the application was filed, the claimed subject matter was in the inventors' possession, conceptually speaking.

4. In particular, I understand the examiner to have concluded that the body of the application does not substantiate the inventors' contemporaneous possession of that aspect of the claimed subject matter reflected in the recitation by claim 1 of a "linear flow rate of at least 1,500 cm/hour." I disagree with this conclusion on factual grounds, which are explicated below and which, in my opinion, would prompt the same conclusion by others in this field.

5. The specification makes it perfectly clear that the term "1.500 cm/hour" refers to "1500 cm/hour" or 25 cm/min. Thus, the application notes that "[o]ne major

advantage of the invention relates to the utility of high flow rates, rather than the conventional ones which amount to about 200 cm/hour." See the published application, US 2007/0092960, at ¶ [0061]. In this manner does the application make it clear that the inventive methodology employs relatively high flow rates, which at least must exceed the "conventional" value of 200 cm/hour.

6. The application also states that, "[p]referably, the linear flow rate may be operated within the range from 1.800 to 10.000 cm/hour, such as within the range of 2.000 to 10.000 cm/hour, such as typically at linear flow rates of about 3000 to 7000 cm/hour." *Id.* Since the range "3000 to 7000 cm/hour" cannot lie between a range of 1.8 and 10 cm/hour, as such, it is immediately clear to me that the recited decimal point (".") must be read as a comma, as I am informed one does with many Danish language texts. When reviewing original claim 13, I likewise understand that the recited "1.500 to 12.000 cm/hour" and "1.800 to 10.000" must be read as "1,500 to 12,000 cm/hour" and "1,800 to 10,000" cm/hour, respectively, so as to encompass the recited "3000 cm/hour."

7. The examples of the application further support this perspective. Example 1 discloses the isolation of lactoferrin using a column with a diameter of 30 cm. *Id.* at [0120]. The example shows that a total volume of 3459 l was processed in 3.26 hours. As this flow rate equates to 1,500 cm/hour, I recognize that the phrase "1.500 cm/hour" in the example denotes "1,500 cm/hour." Similarly, Examples 2, 3, 4, and 12 mention a flow rate of "1,500 cm/hr," *inter alia.*

8. Furthermore, my experience informs me that a linear flow rate of just 1.5 cm/hour (i.e. 2½ mm/minute) is inoperable in the context of expanded-bed technology. Stated simply, a chromatographic bed cannot "expand" at such extremely slow flow rates. Moreover, a flow rate prescribed to a value of three significant figures, i.e., to an accuracy rate of 10 μm or "1½ cm/hour," is unrealistic in this context.

9. From the explicit teachings of the application, therefore, it is readily apparent that the phrase "1.500 cm/hour" in the original specification and claims contains a punctuation

error, and that the decimal point (".") should be read as a comma (","), i.e., "1,500 cm/hour" or "1500 cm/hour."

10. I declare that the statements made herein of my knowledge are true and all statements on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therein.

June 30, 2009

Date

Thierry Burnouf